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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/591,185	06/08/2000	Ronald M. Cook	19079-000310US	2668

7590

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EXAMINER

EPPS, JANET L

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 02/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/591,185	COOK, RONALD M.	
	Examiner	Art Unit	
	Janet Epps	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-61 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32-61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 June 2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Response to Amendment

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 50-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly added claims 50-62 recite wherein "each CHOL interacts with the other CHOL to bring D and Q into operative proximity, thereby enabling transfer of energy from D to Q." However, there is no specific support in the specification as filed that clearly sets forth the above claim language. The specification (page 5, lines 18-20) as filed recites wherein "X and Y are the same or different and are no-nucleotide stabilizing moieties that interact to bring R and Q into operative proximity, thereby enabling transfer of energy from R to Q." In the following paragraph, on the same page (page 5, lines 22-28), the specification as filed recites "[I]n another aspect, the invention provides a CAP probe having the formula:" as recited in claim 50, however, there is no reference in this section of the specification which specifically states that, in regarding the structure on page 5, line 23, that "each CHOL interacts with the other CHOL to bring D and Q into operative proximity, thereby enabling transfer of energy from D to Q." There is no specific reference to either X or Y wherein they are both specifically limited to CHOL, and further that CHOL possess the same properties as those required for the X and Y moieties.

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Therefore, the amendment filed 10-03-01 is objected to under 35 U.S.C. 132 because it introduces new matter into the claims. The added material which is not supported by the original disclosure is as follows: “each CHOL interacts with the other CHOL to bring D and Q into operative proximity, thereby enabling transfer of energy from D to Q.”

Applicant is required to cancel the new matter in the reply to this Office Action.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 32-49 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32, and those claims dependent thereon, claims 2-49, recite “[A] compound having a structure selected from: X-R-A-Q-(Y)_n, R-X-A-(Y)_n-Q, R-X-A-Q-(Y)_n, and X-R-A-(Y)_n-Q.” This phrase is vague and indefinite since it unclear if the compound claimed in the instant case reads on a formula according to one of X-R-A-Q-(Y)_n, R-X-A-(Y)_n-Q, R-X-A-Q-(Y)_n, or X-R-A-(Y)_n-Q, as defined in the specification as filed (page 5, lines 12-15), or on a structure recited in one of these formulas. For example, it is unclear if the compound encompasses a structure according to A, R, Q, X, and Y, or a formula according to X-R-A-Q-(Y)_n, R-X-A-(Y)_n-Q, R-X-A-Q-(Y)_n, and X-R-A-(Y)_n-Q.

Claim 33 recites “said molecular energy donor” in claim 32. There is lack of antecedent basis for this limitation in claim 32.

Claim 34 recites “said molecular energy acceptor” in claim 32. There is lack of antecedent basis for this limitation in claim 32.

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Claim 39 recites "members independently selected from the group consisting phosphodiesters and modified phosphodiesters." This claim appears to recite a Markush group without the proper use of the Markush format. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925).

Claim 41 recites "said nucleic acid sequence" in claim 32. There is lack of antecedent basis for this limitation in claim 32.

Claim 60 recites the limitation "said PEG" in claim 59. There is lack of antecedent basis for this limitation in claim 59.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 32-62 are rejected under 35 U.S.C. 103(a) as being unpatentable for the reasons of record set forth in the Official Action mailed 5-30-01, in the rejection of claims 1-3, 6-11, 13-26, and 28-30 under 35 USC 103(a) over Meade et al. in view of Manoharan et al. and Gold et al. Applicant's arguments filed 10-12-01 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the combination of cited references do not teach wherein "the non-nucleic acid stabilizing moieties (e.g., cholesterol) interact with

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each other to bring the energy donor and the energy acceptor into operative proximity, thereby enabling transfer of energy from the donor to acceptor.” However, contrary to Applicant’s assertions, the combined references, particularly the Meade et al. reference clearly provides sufficient guidance for the successful design of nucleic acid molecules comprising electron donor and electron acceptor moieties covalently bound to the ribose-phosphate backbone of said nucleic acid (Meade et al., col. 5, lines 45-53). Furthermore, Meade et al. teach the detection of electron transfer between electron acceptor/donor pairs covalently linked to a nucleic acid molecule after photoinduction, as an indication of a successful amplification (col. 12, lines 25-40). It is noted that Applicant’s claims are directed to either a product, or methods of using a product having specific properties, however if the prior art teaches or renders obvious the claimed compound, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In the instant case, the prior art clearly suggests, and provides sufficient motivation for the covalent attachment of Cholesterol moieties into two non-terminal positions of a nucleic acid molecule via an organic linker (see Manoharan et al.), and further provides motivation for the addition of an electron donor and an electron acceptor moiety attached to either the 5’ or 3’ terminus of an oligonucleotide. Applicants have not clearly set forth sufficient argument as to why the modified compounds resultant from the combination of Meade et al. in view of Manoharan et al. and Gold et al., would not possess the same properties as those compounds recited in the of the instant claims. Absent evidence of unexpected results, the compounds of Meade et al. in view of Manoharan et al. and Gold et al. have similar properties, and it is deemed that since such is the case, other claimed limitations not

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disclosed are inherent. Sufficient evidence of similarity is present to shift the burden to Applicant to provide evidence that the claimed products are unobviously different than the modified oligonucleotides disclosed in the references described above.

Furthermore, in response to applicant's argument that the references fail to motivate their combination, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). As stated in the prior Office Action, one of ordinary skill in the art would have been motivated to modify the nucleic acid probes of Meade et al. with the modifications of Manoharan et al. and Gold et al. because the modified oligonucleotides of Manoharan et al. and Gold et al. and the nucleic acid probes of Meade et al. are disclosed as useful for the same purposes, particularly for diagnostic purposes, and the modifications of Manoharan et al. and Gold et al. would confer enhanced cellular uptake while not affecting the binding affinity of the nucleic acid probes of Meade et al.

7. Claims 32-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al. (US 5,866,336) in view of Templeton et al. (Nature Biotechnology, 1997, Vol. 15, pages 647-652).

Nazarenko et al. teach a compound having a structure comprising nucleic acid chains, a molecular energy transfer donor which is a fluorophore and a molecular energy acceptor which is a fluorescence quencher wherein the nucleic acids interact to bring the donor and acceptor into operative proximity to thereby enable transfer of energy between the donor and acceptor (col. 12, lines 36-52 and Figure 1). Nazarenko et al. do not teach a non-nucleic acid moiety that stabilizes

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the energy transfer donor and acceptor into operative proximity. However, non-nucleic acid moieties and in particular hydrocarbons and steroids were known in the art to stabilize structure of nucleic acid compounds.

Templeton et al. teach a compound comprising nucleic acids and cholesterol (a steroid) wherein the cholesterol stabilizes the complex (page 651, right col.).

It would have been obvious to one of ordinary skill in the art, at the time of filing, to modify the compounds of Nazarenko et al. with the cholesterol modifications taught by Templeton et al. for the expected benefit of increased stability and efficient targeting of the nucleic acids in the compounds to cells as taught by Templeton et al. (page 651, right col., 3rd para., lines 1-2). One of ordinary skill in the art would have been motivated to modify the compounds of Nazarenko et al. with the teachings of Templeton et al. since compounds modified as per the teachings of these references would have enhanced cellular properties in comparison to unmodified oligonucleotides.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

9. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C.

122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claim 32 is rejected under 35 U.S.C. 102(b) as being anticipated by Nazarenko et al.

Due to the ambiguity regarding the claim language recited in claim 32 (see rejection under 35 USC 112, 2nd paragraph), claim 32 can be interpreted as reading on any compound having a structure according to A, R, Q, X, and Y, or to a formula according to X-R-A-Q-(Y)_n, R-X-A-(Y)_n-Q, R-X-A-Q-(Y)_n, and X-R-A-(Y)_n-Q.

Nazarenko et al. is applied as 102(b) to claim 32 to the extent that claim 32 reads on a “structure” according to A, R, Q, X, or Y. As stated above, Nazarenko et al. teach a compound having a structure comprising nucleic acid chains, a molecular energy transfer donor which is a fluorophore and a molecular energy acceptor which is a fluorescence quencher wherein the nucleic acids interact to bring the donor and acceptor into operative proximity to thereby enable transfer of energy between the donor and acceptor (col. 12, lines 36-52 and Figure 1). Therefore, Nazarenko et al. discloses compounds having a structure according to A, R, and Q as defined in claim 32.

Nazarenko et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

11. Claim 32 is rejected under 35 U.S.C. 102(e) as being anticipated by Meade et al.

If claim 32 is interpreted as set forth in the above rejection, the instant claim is anticipated by Meade et al. to the extent that Meade et al. discloses nucleic acid covalently linked to electron acceptor/donor pairs (col. 12, lines 25-40). Meade et al. discloses compounds having a structure according to A, R, and Q as defined above.

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Meade et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


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13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps whose telephone number is 703-308-8883. The examiner can normally be reached on Mondays through Friday, 9:00AM to 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps
Patent Examiner
February 5, 2002



SEAN MCGARRY
PRIMARY EXAMINER